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4. Topic of Research   : Design of Potential Antifungals against *Candida albicans* (*C. albicans*)

FINDING

The present study describes our current knowledge of transition from commensal to pathogen, host-pathogen interaction and *C. albicans* infection. We investigated current antifungal treatments, mechanisms of action, evolution of drug resistance in experimental populations and clinical settings. By tackling the high morbidity-mortality rates associated with candidiasis and therapeutic resistance as an evolutionary issue, there is potential to progress the effectiveness of recent disease management and accelerate the advancement of new remedial approach. Thus, study enlightens the promising procedures to design the potent antifungal to obstruct the advancement of drug resistance against *C. albicans*.

To comprehend the cumulative burden of *Candida* species and candidiasis with antifungal resistance in Indian population, a systematic review was conducted. The review of 106 included studies based upon the inclusion and exclusion criteria revealed *C. albicans* as highly prevalent and antifungal resistant species of India. Thereafter, we aimed to identify potent drug target against *C. albicans*. Comparative and subtractive genomics with prioritization analysis revealed 13 virulent proteins as potent target for drug designing. Homology modeling of virulent targets was revealed that out of 13 targets, template structure was present only for 3 *i.e.,* TRR1, TOM40 and YHB1. All three were validated using molecular dynamic simulation to understand the stability of the molecules in biological environment. Further, repurposing of FDA approved drugs against 3 selected targets was performed *via* high throughput virtual screening. Molecular dynamic simulation revealed the best binding mode and stability of each complex. The RMSD, RMSF and Radius of gyration disclosed "TRR1 + Arbutamine" as best "Target + Inhibitor" complex followed by TOM40 + Hydroxychloroquine. Post simulation analysis also confirmed the TRR1-Arbutamin as best, stable and highly effective pair of drug-target complex. Hence, the study suggested *in-vitro* antifungal experiments to control the candidiasis. Arbutamin followed by Hydroxychloroquine had a noteworthy inhibitory result on biofilm development and emission of extracellular enzymes (proteinases and phospholipases). Adhesion of cells also identified significantly reduced in case of Arbutamin followed by Hydroxychloroquine. Similar pattern is identified in yeast to hyphal transition. In comparison, Arbutamin found to be more effective as antifungal instead of Hydroxychloroquine. Finally, the study proposed TRR1 and Arbutamin as potent drug-target complex to treat the candidiasis caused by *C. albicans*.